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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Tomi Jarvinen

HORMOS-019

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7590

09/24/2010

JAMES C. LYDON

100 DAINGERFIELD ROAD

SUITE 100

ALEXANDRIA, VA 22314

EXAMINER

GOON, SCARLETT Y

ART UNIT

PAPER NUMBER

1623

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/521,761	Applicant(s) JARVINEN ET AL.	
	Examiner SCARLETT GOON	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 September 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>9 September 2010 and 12 September 2010</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Office Action is in response to Applicants' Remarks filed on 9 September 2010.

The Declaration of Mr. Jukka Mönkkönen (not an inventor), submitted by Applicants on 12 September 2010 under 37 CFR § 1.132, are acknowledged and will be further discussed below.

Claims 13-20 are currently pending and are examined on the merits herein.

Priority

This application is a National Stage entry of PCT/FI03/00511 filed on 24 June 2003 and claims priority to Finland foreign application 20021545 filed on 29 August 2002. A certified copy of the foreign priority document in English has been received.

Information Disclosure Statement

The information disclosure statements (IDS) dated 9 September 2010 and 12 September 2010 comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. Accordingly, they have been placed in the application file and the information therein has been considered as to the merits.

Applicants are requested to note that references BM and BN on the IDS dated 12 September 2010 were crossed-out because these references were previously cited on the IDS dated 9 September 2010, and considered by the Office.

The following rejections of record in the previous Office Action are maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Section [0001]

Claims 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over PG Pub No. US 2002/0061854 A1 to Ahotupa *et al.* (of record), in view of journal publication by Loftsson *et al.* (of record).

Ahotupa *et al.* teach a pharmaceutical preparation comprising an effective amount of hydroxymatairesinol, a geometric isomer or a stereoisomer thereof, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier (paragraph 0014). Ahotupa *et al.* also teach a food product comprising hydroxymatairesinol, a geometric isomer or a stereoisomer thereof, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier (paragraph 0015 and 0016). The pharmaceutical preparation is preferably an oral formulation. Typical dosage forms include, but are not limited to, oral dosage forms such as powders, granules, capsules, tablets, caplets, lozenges, liquids, elixirs, emulsions and suspensions. All such dosage forms may include conventional carriers, diluents, excipients, binders and additives known to those skilled in the medicinal and pharmaceutical arts (paragraph 0025). The pharmaceutical carriers typically employed may be solid or liquid. Thus, for example, solid carriers include polysaccharides, while liquid carriers include aqueous solutions of salts, polysaccharides, complexing agents, surfactants, syrups, vegetable oils and certain alcohols (paragraph 0026). However, any pharmaceutically acceptable solid or liquid carrier can be used in the pharmaceutical preparation, except that the formulation

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cannot be a mixture of only the active agent and plain water (paragraph 0026). When the composition is used as an additive to foods, the carrier can be any non-toxic solid or liquid carrier acceptable for use in food and suitable to be admixed with hydroxymatairesinol (paragraph 0027). Typical solid carriers includes polysaccharides and typical liquid carriers include aqueous solutions of salts, polysaccharides, complexing agents, surfactants, syrups, vegetable oils and certain alcohols (paragraph 0028). However, any acceptable solid or liquid carrier can be used in the food additive, except that the formulation cannot be a mixture of only the active agent and plain water (paragraph 0028). The food product is preferably a functional food, a nutritional supplement, a nutrient, a pharmafood, a nutraceutical, a health food, a designer food or any food product (paragraph 0029). The composition may also be used as a dietary supplement (paragraph 0069).

Although Ahotupa *et al.* teach a pharmaceutical composition comprising hydroxymatairesinol in combination with a pharmaceutically acceptable carrier that includes polysaccharides, the teachings of Ahotupa *et al.* differ from that of the instantly claimed invention in that Ahotupa *et al.* do not expressly teach cyclodextrins as the polysaccharide carrier.

Loftsson *et al.* teach that cyclodextrins are frequently regarded as a new group of pharmaceutical excipients, although they have been known for over 100 years. Highly purified cyclodextrins and cyclodextrin derivatives are well suited as pharmaceutical excipients (p. 1017, column 1). Cyclodextrins can interact with appropriately sized molecules to result in the formation of inclusion complexes. These noncovalent

complexes offer a variety of physiochemical advantages over the unmanipulated drugs including the possibility for increased water solubility and solution stability (p. 1017, abstract). Additionally, the cyclodextrins can be used to increase bioavailability of the drugs, or be used to convert liquid drugs into microcrystalline powders or prevent drug-drug or drug-additive interactions (p. 1017, column 2, first bridging paragraph). The most common cyclodextrins include the natural cyclodextrins, α -, β -, and γ -cyclodextrin (p. 1017, column 2, second paragraph). The natural cyclodextrins can be modified to increase their water solubility, such as by alkylation or hydroxyalkylation of the cyclodextrin hydroxyl groups (p. 1018, column 1). Examples of modified cyclodextrins are shown in Table 2, including alkylated and hydroxyalkylated derivatives (p. 1019, column 1). The most common pharmaceutical application of cyclodextrins is to enhance drug solubility in aqueous solutions (p. 1020, column 2, first paragraph). The solubilizing effects of various cyclodextrins on three different drugs are shown in Table 5 (p. 1021). Cyclodextrins are thus useful as tools to generate aqueous drug solutions without the use of organic cosolvents, surfactants, or lipids, as formulation adjuncts which increase dissolution rates and oral bioavailability of solid drug complexes, and as materials used to generate safe iv dosage forms intended to provide important pharmacokinetic information or act as potential drug products per se (p. 1024, column 2).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Ahotupa *et al.*, concerning a pharmaceutical preparation comprising an effective amount of hydroxymatairesinol, a geometric isomer

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or a stereoisomer thereof, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier, with the teachings of Loftsson *et al.*, regarding the use of cyclodextrins as pharmaceutical excipients. Since Ahotupa *et al.* teach that a pharmaceutically acceptable carrier includes polysaccharides known in the art, and Loftsson *et al.* teach that cyclodextrins are useful as pharmaceutical excipients, one of ordinary skill in the art would have been motivated to combine the teachings and select any of the cyclodextrins as the pharmaceutically acceptable carrier in the pharmaceutical preparation disclosed by Ahotupa *et al.*, in order to receive the expected benefit, as suggested by Loftsson *et al.*, that the use of cyclodextrins as a pharmaceutically acceptable excipient offers many advantages, including their ability to increase drug bioavailability, generate aqueous drug solutions without the use of organic cosolvents, surfactants, or lipids, as formulation adjuncts which increase dissolution rates and oral bioavailability of solid drug complexes, and as materials used to generate safe iv dosage forms intended to provide important pharmacokinetic information or act as potential drug products per se (p. 1024, column 2). Furthermore, as Ahotupa *et al.* teach that any pharmaceutically acceptable solid or liquid carrier can be used in the pharmaceutical preparation, such as polysaccharides, and Loftsson *et al.* teach that cyclodextrins are known pharmaceutically acceptable excipients, one of ordinary skill in the art would have had a reasonable expectation of success in formulating a pharmaceutical composition comprising hydroxymatairesinol and a cyclodextrin, thereby forming an inclusion complex.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Section [0002]

Claims 13-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over PG Pub No. US 2001/0016590 A1 to Ahotupa *et al.* (of record), in view of journal publication by Loftsson *et al.* (of record).

Ahotupa *et al.* teach a pharmaceutical preparation comprising an effective amount of hydroxymatairesinol, a geometric isomer or a stereoisomer thereof, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier (paragraph 0013). The pharmaceutical preparation is preferably an oral formulation (paragraph 0023). Ahotupa *et al.* also teach a food product comprising hydroxymatairesinol, a geometric isomer or a stereoisomer thereof, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier (paragraph 0014). The food product is preferably a functional food, a nutritional supplement, a nutrient, a pharmafood, a nutraceutical, a health food, a designer food or any food product (paragraph 0025). The composition may also be used as a dietary supplement (paragraph 0080).

Although Ahotupa *et al.* teach a pharmaceutical composition comprising hydroxymatairesinol in combination with a pharmaceutically acceptable carrier, the teachings of Ahotupa *et al.* differ from that of the instantly claimed invention in that Ahotupa *et al.* do not expressly teach cyclodextrins as the carrier.

The teachings of Loftsson *et al.* were as disclosed in section [0001] above of the claim rejections under 35 USC § 103.

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings of Ahotupa *et al.*, concerning a pharmaceutical preparation comprising an effective amount of hydroxymatairesinol, a geometric isomer or a stereoisomer thereof, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier, with the teachings of Loftsson *et al.*, regarding the use of cyclodextrins as pharmaceutical excipients. Since Loftsson *et al.* teach that cyclodextrins are useful as pharmaceutical excipients, one of ordinary skill in the art would have been motivated to combine the teachings and select any of the cyclodextrins as the pharmaceutically acceptable carrier in the pharmaceutical preparation disclosed by Ahotupa *et al.*, in order to receive the expected benefit, as suggested by Loftsson *et al.*, that the use of cyclodextrins as a pharmaceutically acceptable excipient offers many advantages, including their ability to increase drug bioavailability, generate aqueous drug solutions without the use of organic cosolvents, surfactants, or lipids, as formulation adjuncts which increase dissolution rates and oral bioavailability of solid drug complexes, and as materials used to generate safe iv dosage forms intended to provide important pharmacokinetic information or act as potential drug products per se (p. 1024, column 2). Furthermore, as Ahotupa *et al.* teach that any pharmaceutically acceptable solid or liquid carrier can be used in the pharmaceutical preparation and Loftsson *et al.* teach that cyclodextrins are known pharmaceutically acceptable excipients, one of ordinary skill in the art would have had a

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reasonable expectation of success in formulating a pharmaceutical composition comprising hydroxymatairesinol and a cyclodextrin, thereby forming an inclusion complex.

Thus, the claimed invention as a whole is *prima facie* obvious over the combined teachings of the prior art.

Response to Arguments

Applicants' arguments, filed 9 September 2010, and the Declaration of Mr. Jukka Mönkkönen, submitted on 9 September 2010 under 37 CFR § 1.132, with respect to the rejection of claims 13-20 under 35 USC § 103(a) as being unpatentable over PG Pub No. US 2002/0061854 A1 to Ahotupa *et al.*, in view of journal publication by Loftsson *et al.*, and independently over PG Pub No. US 2001/0016590 A1 to Ahotupa *et al.*, in view of journal publication by Loftsson *et al.*, have been fully considered but they are not persuasive.

Applicants argue that the cited combination of references fails to raise a *prima facie* case of obviousness because one of ordinary skill in the art would not have a reasonable expectation of success in preparing the claimed complex from the cited references, or that it would work for its intended purpose. Applicants argue that the teachings of Loftsson *et al.* is a general review of pharmaceutical uses of cyclodextrin complexes, and fails to disclose or suggest an inclusion complex of a cyclodextrin and HMR. Specifically, Applicants argue that Loftsson's express teaching that the "prediction of compound solubilization by cyclodextrins continues to be highly empirical"

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suggests that cyclodextrin inclusion complexes is an unpredictable art, both with respect to complex formation and guest molecule stability. Applicants further submitted a Declaration by Mr. Mönkkönen under 37 C.F.R. § 1.132 to substantiate the unpredictability of the art. Mr. Mönkkönen states that although CDs are known to retard degradation of a drug, they are also known to have no effect on their stability, or even to accelerate degradation of the drug, citing several publications to support his argument. Thus, Applicants argue that this contributes to the unpredictability of the art. Mr. Mönkkönen conclude by saying, “[i]n my opinion, one of ordinary skill would not have a reasonable expectation of success that cyclodextrins would form inclusion complexes with lignans and lignan esters from the Ahotupa references in view of Loftsson *et al.*”

Applicants' arguments, the Declaration of Mr. Mönkkönen, and the cited publications, have been carefully reviewed but are not considered persuasive. In response to Applicants' argument that Loftsson *et al.* fail to disclose or suggest an inclusion complex of a cyclodextrin and HMR, Applicants are requested to note that an obviousness “analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ.” *KSR*, 550 U.S. at 418.

In response to Applicants' argument that the teachings of Loftsson *et al.* suggest that cyclodextrin inclusion complexes is an unpredictable art, Applicants are requested to note that the courts have held that obviousness does not require absolute predictability, only a reasonable expectation of success, i.e., a reasonable expectation

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of obtaining similar properties. See, e.g., *In re O 'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). See also MPEP § 2143.06(e). With respect to the instant rejections, one of ordinary skill in the art would have a reasonable expectation of success because, although Loftsson *et al.* do state that the prediction of compound solubilization by CDs continue to be highly empirical, as noted by Applicants, Applicants fail to further note that in the same thought, Loftsson *et al.* continue to state that "[however,] various historical observations permit several general statements," going on to teach the various generalizations regarding the relationship between solubility of a drug and its relative solubility enhancement as a CD complex, how CD derivatives of lower molar substitution are better solubilizers than the same type of derivatives of higher molar substitution, and how charged CDs are powerful solubilizers. Thus, Loftsson *et al.* acknowledge that generalizations regarding the complexation of a drug with CD can be used as guidelines for the preparation of a CD inclusion complex of a drug. Furthermore, in concluding their discussion on methods useful in the optimization of CD complexation efficacy of drugs, Loftsson *et al.* teach that "[b]oth parent and modified cyclodextrins are rapidly being assimilated into the formulator's armamentarium," that "[i]n the United States, a monograph for β -cyclodextrins is available in the Pharmacopoeia." Loftsson *et al.* also teach that a monograph for β -cyclodextrins "is already in the Japanese Pharmacopoeia, and it will soon appear in the European Pharmacopoeia". Additionally, Loftsson *et al.* teach that the use of cyclodextrin as an excipient is available in the *Handbook of Pharmaceutical Excipients*. Applicants are requested to note that the teachings of Loftsson *et al.* occurred in 1996,

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six years prior to the priority date of Applicants' instantly claimed invention. Due to the extensive teachings of the use of cyclodextrins as excipients, as well as their disclosure in various Pharmacopoeia and books discussing pharmaceutical excipients, it is the Office's position that the selection of cyclodextrins as a polysaccharide excipient with HMR, at the appropriate concentrations to form an inclusion complex, is routine in the art, and not considered an area of unpredictable art, as argued by Applicants. Rudnic *et al.* teach in "Remington's Pharmaceutical Sciences" (PTO-892, Ref. A, p. 1633, top section) that it is known that additives are included in formulations to enhance the physical appearance, improve the stability, and aid in the disintegration of a drug after administration, and that these supposedly inert ingredients have been shown in some cases to influence the release of the drug substances. Therefore, Rudnic *et al.* teach that "care must be taken in the selection and evaluation of additives and preparation methods" of the drug, suggesting that the selection of the optimal pharmaceutical excipients to use in a drug formulation is routine in the art. Moreover, Wade *et al.* provide in the 1994 publication entitled "Handbook of Pharmaceutical Excipients" (PTO-892, Ref. B), a publication also cited by Loftsson *et al.*, a comprehensive, uniform guide to the uses, properties, and safety of pharmaceutical excipients (p. xi of preface, column 2, last paragraph). The handbook includes a monograph on cyclodextrins. Wade *et al.* acknowledge that excipients are known to exert effects on the bioavailability, bioequivalence, and stability of formulations, and that relatively small variations in the physical properties of an excipient can produce significant differences in the behavior of formulated products (p. xi of preface, paragraph bridging columns 1 and 2). Thus,

Wade *et al.* state that the publication “is an essential reference source for those involved in the development, production, or control of pharmaceutical preparations” (p. xi of preface, column 2, last paragraph). Similar to Rudnic *et al.*, the teachings of Wade *et al.* suggest that the selection of an appropriate and optimal pharmaceutical excipient is routine in the art. Thus, the Office maintains that one of ordinary skill in the art would have a reasonable expectation of success in forming a cyclodextrin inclusion complex of HMR based on the combined teachings of the prior art.

As Ahotupa *et al.* teach that typical solid carriers that could be used for formulation of HMR include polysaccharides, and Loftsson *et al.* teach that cyclodextrins are useful as pharmaceutical excipients, such as the natural cyclodextrins, α -, β -, and γ -cyclodextrin, which are polysaccharides, one of ordinary skill in the art would have been motivated to select CDs as the polysaccharide excipient, in order to receive the expected benefit, as taught by Loftsson *et al.*, that the use of cyclodextrins as a pharmaceutically acceptable excipient offers many advantages, including their ability to increase drug bioavailability, generate aqueous drug solutions without the use of organic cosolvents, surfactants, or lipids, as formulation adjuncts which increase dissolution rates and oral bioavailability of solid drug complexes, and as materials used to generate safe iv dosage forms intended to provide important pharmacokinetic information or act as potential drug products per se (p. 1024, column 2). Moreover, even in the absence of express teachings from Ahotupa *et al.* to use CDs as a polysaccharide excipient, in view of the significant advantages taught by Loftsson *et al.* regarding the use of CDs as a pharmaceutical excipient, it would have been at least

prima facie obvious for one of ordinary skill in the art to try using CDs as an excipient, at least with the commonly used CDs cited by Loftsson *et al.*

Therefore, since Ahotupa *et al.* disclose the formulation of HMR with excipients, such as polysaccharides, and Loftsson *et al.* teach that common CDs include the natural cyclodextrins, α -, β -, and γ -cyclodextrin, and the substituted CDs in Table 2, it would have been *prima facie* obvious for one of ordinary skill in the art to at least try formulation of HMR with these common CDs. Under the current legal standard for obviousness (*KSR*, 550 U.S. at ___, 82 USPQ2d at 1396), since there is a finite number of compounds to try, it would have been *prima facie* obvious for one of ordinary skill in the art to try making such a composition, with the reasonable expectation that it would result in a complexation of HMR with the CD. The rationale to support a conclusion that the claim would have been obvious is that “a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely that product [was] not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103.” *KSR*, 550 U.S. at ___, 82 USPQ2d at 1397. See also MPEP § 2143.

Mr. Mönkkönen additionally state in the Declaration that “the scientific knowledge supports the fact that prediction of CD complexation is very difficult without laborious experiments in the laboratory,” again citing several publications. These arguments and the publication are not persuasive because, as discussed previously, one of ordinary skill in the art only needs a reasonable expectation of success, i.e., a reasonable

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expectation of obtaining similar properties. See, e.g., *In re O 'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). See also MPEP § 2143.06(e). As the different effects of drug complexation with a CD are known, and Loftsson *et al.* provide some guidelines as to how to select the appropriate CD and concentration for formation of the inclusion complex, it is the Office's position that that one of ordinary skill in the art would have a reasonable expectation of success. Thus, contrary to Mr. Mönkkönen's statement that CD complexation is very difficult without laborious experiments, in view of the teachings of Loftsson *et al.*, and the extensive availability of teachings on the use of CDs as a pharmaceutical excipient, including the numerous publications cited by Applicants which span the year from 1990-2005, the complexation of CD with HMR is considered routine in the art to a formulation chemist of ordinary skill in the art. The formation of an inclusion complex of a drug with a CD is not an unpredictable art, but rather, a field that has been extensively studied. The amount of work required, namely, the selection of the appropriate CD, depending on factors such as the charge and hydrophobicity of the drug, and the determination of the appropriate ratio of drug to CD necessary to form an inclusion complex, are considered routine in the art.

Therefore, Applicants' arguments and the Declaration of Mr. Mönkkönen are ineffective to rebut the *prima facie* case herewith.

The rejections are still deemed proper and therefore maintained.

Conclusion

In view of the rejections to the pending claims set forth above, no claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SCARLETT GOON whose telephone number is 571-270-5241. The examiner can normally be reached on Mon - Thu 7:00 am - 4 pm and every other Fri 7:00 am - 12 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Shaojia Anna Jiang/
Supervisory Patent Examiner, Art Unit 1623

/SCARLETT GOON/
Examiner
Art Unit 1623